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Clinical study on the effect of remifentanil patient-controlled intravenous labor analgesia compared to patient-controlled epidural labor analgesia

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ABSTRACT

Objectives: This study aims to investigate the safety and efficacy of remifentanil for patient-controlled intravenous labor analgesia as an alternative to the patient-controlled epidural labor analgesia.

Material and Methods: Out of 453 parturients who volunteered for labor analgesia and were selected as research objects, 407 completed the trial. They were divided into the research group (n = 148) and the control group (n = 259; patient-controlled epidural analgesia). In the research group, the first dose of remifentanil, the background dose and the patient-controlled analgesia (PCA) dose were 0.4 μg/kg, 0.04 μg/min and 0.4 μg/kg, respectively, with a lockout interval of 3 min. The control group was given epidural analgesia. The first dose and background dose were 6–8 mL, and PCA dose and the locking time of analgesia pump were 5 mL and 20 min, respectively. The following indexes of the two groups were observed and recorded: the analgesic and sedative effects on parturient, labor process, forceps delivery, cesarean section rate and adverse reactions, and maternal and neonatal conditions.

Results: (1) The onset time of analgesia in the research group was (0.97 ± 0.08) min, which was noticeably shorter than that in the control group ([15.74 ± 1.91] min), with a statistically significant difference ($t = -93.979$, $p = 0.000$). (2) There was no significant difference in the labor process, forceps delivery, cesarean section rate and neonatal condition between the two groups ($p > 0.05$).

Conclusions: Remifentanil patient-controlled intravenous labor analgesia has the advantage of rapid onset of labor analgesia. Although its analgesic effect is not as accurate and stable as epidural patient-controlled labor analgesia, it shows a high level of maternal and family satisfaction.

Key words: remifentanil; epidural analgesia; patient-controlled; epidural infusion; analgesia

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INTRODUCTION

Achieving a satisfactory labor analgesia effect is very important in the process of parturient delivery. Patient-controlled epidural labor analgesia is recognized as the most effective method of labor analgesia [1]. However, if there is a need for labor analgesia, but there are contraindications of intraspinal block, refusal of epidural puncture or unsatisfactory coordination of anesthesia position, another suitable, safe and effective labor analgesia method should be selected to replace epidural patient-controlled labor analgesia [2]. In the studies performed so far to compare the effects of remifentanil in patient-controlled labor analgesia and epidural patient-controlled labor analgesia, the sample size has been small [3, 4]. Thus, in the present study, we included a large sample size to evaluate the safety and effectiveness of remifentanil intravenous patient-controlled labor analgesia. We investigated the satisfaction of parturient and their families with respect to the effect of labor analgesia to gain a better insight on the feasibility of remifentanil patient-controlled intravenous labor analgesia as an alternative to patient-controlled epidural labor analgesia.

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MATERIAL AND METHODS

Materials

Four-hundred and fifty-three parturients who gave birth in the Shanghai First Maternity and Infant Hospital and voluntarily asked for labor analgesia were selected as the study subjects. Of these, 407 (89.8%) parturients who delivered from May to November 2019 completed the trial according to the mode of labor analgesia voluntarily chosen by them. Their age ranged from 21 to 43 years old, with an average of 29.3 ± 2.7 years old. The gestational weeks ranged from 37.0 to 42.3, with an average of 39.3 ± 1.1 weeks. They were divided into a research group (n = 148; patient-controlled intravenous analgesia with remifentanil) and a control group (n = 259; patient-controlled epidural analgesia). There was no significant difference in age, weight, height, body mass index and gestational age between the two groups ($p > 0.05$), as shown in Table 1. The inclusion criteria of this study are as follows: single pregnancy, full-term pregnancy, vaginal trial delivery, American Society of Anesthesiologists (ASA) grade I–II, primipara, voluntary labor analgesia. The exclusion criteria are as follows: parturients with pathological obstetric factors, an opioid drug abuse history, remifentanil contraindications, other opioid drugs (*e.g.*, pethidine, *etc.*) used within eight hours before labor analgesia, spinal deformity, and contraindications of intraspinal block. The procedure followed in this study was in line with the ethical standards formulated by the human experimental Committee of Shanghai First Maternity and Infant Hospital. The informed consent was obtained from the subjects in the groups. They signed informed consent forms for clinical research and labor analgesia.

Table 1. Comparison of basic clinical data between research group and control group

Characteristics	Research group (n = 148)	Control group (n = 259)	p value
Age [years]	29.7 ± 3.5	29.5 ± 3.2	0.11
Weight [kg]	71.4 ± 9.3	72.3 ± 5.7	0.15
Height [cm]	161.2 ± 3.5	162.3 ± 3.2	0.21
BMI [kg/m^2]	27.6 ± 3.1	27.5 ± 1.8	0.73
Gestational age [weeks]	39.3 ± 1.2	39.1 ± 1.3	0.35

BMI — body mass index

Methods

Methods of labor analgesia in research group and control group

The research group and the control group entered the delivery room when the cervical dilatation was ≥ 3 cm and were provided with doula one-to-one support. They were subjected to constant monitoring of maternal vital signs, fetal heart rate and uterine contraction. After the parturient entered the delivery room, the vein was opened. In case the fetal ECG monitoring showed abnormality, the parturient was given 3 L/min oxygen through nasal catheter to ensure safety. The subjects in the research group were given remifentanil intravenous patient-controlled analgesia (PCA). The concentration of remifentanil was 20 μg/mL, and it was intravenously injected when the uterine contraction was coming. The first dose of remifentanil, background dose and the PCA dose were 0.4 μg/kg, 0.04 μg/min and 0.4 μg/kg, respectively, where the locking time of analgesia pump (ZZB-150, Aipeng Medical Technology Co., Ltd, Jiangsu, China) was 3 min. According to the guidance of maternal pain intolerance, PCA should be initiated about the time the uterine contraction is started. The subjects in the control group were given epidural analgesia. The median approach of L2–3 intervertebral space was selected for epidural puncture and catheterization. The first dose and background dose of the pump liquid (0.3 μg/mL sufentanil + 0.1% ropivacaine) were 6–8 mL, and PCA dose and the locking time of analgesia pump were 5 mL and 20 min, respectively. The analgesia pump was stopped at the end of the first stage of labor in both groups. An amount of 1 mL of umbilical artery (UA) blood was drawn immediately for blood gas analysis once the fetus was delivered.

Observation indexes of the research group and control group

The following observational indexes were followed. 1) Continuous monitoring and recording of the vital signs, including blood pressure, heart rate, respiratory rate and percutaneous pulse oxygen saturation (SpO_2) before analgesia, at the onset of analgesia, and at 1, 2 and 3 h after analgesia. 2) The onset time of analgesia from the first dose to the obvious relief of pain in the two groups was observed. 3) Visual analogue scale (VAS) was used to evaluate the degree of pain before analgesia, at the onset of analgesia and at 1, 2, and 3 h after analgesia in the two groups, where the score of 0 indicated painless and 10 meant the most painful. 4) Ramsay score was employed to evaluate the degree of sedation before analgesia, at the onset of analgesia, and at 1, 2, and 3 h after analgesia. A score of 2–3 meant mild sedation; 4 indicated deep sedation, and 5–6 showed excessive sedation. 5) The first, the second and the third stages of labor, the use of oxytocin, and whether forceps midwifery or cesarean section was used were recorded. 6) Apgar score and UA blood gas analysis were recorded at 1 min and 5 min after birth. 7) The incidence of adverse reactions, such as dizziness, vomiting, respiratory depression, excessive sedation, pruritus, and numbness of the lower limbs of the two groups were observed on the first day of postpartum follow-up. 8) At the end of the delivery, the mothers and their family members evaluated the satisfaction of labor analgesia effect by the satisfaction scores of 1 (very satisfied), 2 (satisfied),

3 (generally satisfied), 4 (dissatisfied) and 5 (very dissatisfied). The total satisfaction (*Y*) is calculated based on the following equation.

$$Y = \frac{A_1 + A_2}{A} \times 100\%$$

where A_1, A_2, and A are the numbers of scores of very satisfied, generally satisfied and total, respectively.

Methods of statistical analysis

The minimum sample size of this study to meet the requirement of statistical test was determined by using Size software (2.0). Statistical Package for the Social Sciences (SPSS) (17.0) was used to analyze the data. Firstly, the distribution status of each measurement data was analyzed, and measurement data with a normal distribution was represented by $\bar{\chi} \pm s$. The t-test was employed to compare the basic clinical data, Ramsay score, and VAS score between the two groups. For the percentages of vaginal delivery rate, forceps delivery rate, cesarean section rate, oxytocin use rate and analgesic effect satisfaction rate (%), the χ^2 test was used for comparison between the two groups. $P < 0.05$ was considered statistically significant.

RESULTS

Comparison of basic clinical data between research group and control group

According to Table 1, there was no significant difference in age, weight, height, body mass index, and gestational weeks between the research group and the control group ($p > 0.05$).

Comparison of vital signs between the research group and the control group

According to Table 2, there were no notable differences in mean arterial pressure, heart rate, respiratory rate and SpO_2 between the research group and the control group

Table 2. Comparison of vital signs of parturient in the research and the control groups before analgesia, onset time of analgesia, and 1, 2, and 3 h after analgesia

Characteristics	Research group (n = 148)	Control group (n = 259)	p value
Mean arterial pressure [mmHg]			
Before analgesia	86.57 ± 7.65	86.38 ± 7.67	0.80
Onset time of analgesia	86.62 ± 7.21	85.69 ± 7.39	0.21
After analgesia 1 h	86.85 ± 7.35	85.68 ± 7.67	0.12
After analgesia 2 h	85.68 ± 7.49	85.65 ± 7.36	0.97
After analgesia 3 h	86.95 ± 7.02	86.09 ± 7.65	0.25
Heart rate [bpm]			
Before analgesia	84.03 ± 6.96	84.34 ± 6.66	0.65
Onset of analgesia	83.31 ± 7.16	83.49 ± 6.91	0.79
After analgesia 1 h	84.21 ± 6.82	83.60 ± 6.65	0.37
After analgesia 2 h	86.58 ± 6.88	84.26 ± 7.02	0.01
After analgesia 3 h	86.62 ± 6.85	84.53 ± 6.83	0.02
Respiratory rate/[times/min]			
Before analgesia	18.04 ± 1.67	17.86 ± 1.57	0.26
Onset time of analgesia	18.00 ± 1.82	17.82 ± 1.66	0.29
After analgesia 1 h	18.05 ± 1.57	18.05 ± 1.68	1.00
After analgesia 2 h	18.26 ± 1.60	18.00 ± 1.82	0.14
After analgesia 3 h	18.21 ± 1.66	17.95 ± 1.68	0.12
SpO_2 [%]			
Before analgesia	98.73 ± 0.49	98.59 ± 0.63	0.47
Onset of analgesia	98.45 ± 1.09	98.57 ± 0.63	0.21
After analgesia 1 h	98.62 ± 0.88	98.69 ± 0.86	0.42
After analgesia 2 h	98.58 ± 0.78	98.78 ± 0.49	0.15
After analgesia 3 h	98.82 ± 0.52	98.89 ± 0.36	0.13

Values are expressed as mean (SD). Values in bold are statistically different; SpO_2 — Hemoglobin oxygen saturation by pulse oximetry, SD — standard deviation; *The difference was significant, if $p < 0.05$ (Student's t-test)

Table 3. Comparison of analgesic and sedative effects between the research group and the control group			
Characteristics	**Research group (n = 148)**	**Control group (n = 259)**	**p value**
Onset time of analgesia/min	0.97 ± 0.08	15.74 ± 1.91*	< 0.01*
Ramsay score			
Before analgesia	1.05 ± 0.52	1.08 ± 0.48	0.56
Onset of analgesia	2.39 ± 0.57	1.86 ± 0.35*	< 0.01*
After analgesia 1 h	2.29 ± 0.36	1.89 ± 0.38*	< 0.01*
After analgesia 2 h	1.98 ± 0.58	2.02 ± 0.24	0.42
After analgesia 3 h	1.86 ± 0.52	1.85 ± 0.53	1.00

Values are expressed as mean (SD). Values in bold are statistically different; SD — standard deviation; *The difference was significant, if $p < 0.05$ (Student's t-test)

Table 4. Comparison of VAS scores between the two groups of parturients at different time points			
Characteristics	**Research group (n = 148)**	**Control group (n = 259)**	**p value**
Before analgesia	8.7 ± 1.4	8.6 ± 1.6	0.43
Onset of analgesia	4.1 ± 1.7*	2.9 ± 1.2	< 0.01*
After analgesia 1 h	4.3 ± 1.5*	3.2 ± 1.3	< 0.01*
After analgesia 2 h	5.3 ± 1.4*	3.3 ± 1.2	< 0.01*
After analgesia 3 h	5.6 ± 1.3*	3.5 ± 1.1	< 0.01*

Values are expressed as mean (SD). Values in bold are statistically different; SD — standard deviation; *The difference was significant, if $p < 0.05$ (Student's t-test)

before analgesia, at the onset of analgesia or at 1, 2, and 3 h after analgesia ($p > 0.05$).

Comparison of analgesic and sedative effects between the research group and the control group

According to Table 3, the onset time of analgesia in the research group was significantly shorter than that in the control group ($t = –93.979$, $p < 0.05$). The Ramsay scores at the onset of analgesia and one hour after analgesia in the research group were substantially higher than those in the control group, and the differences were highly significant ($t = 9.997, 10.411$, $p = 0.000$). There were no significant differences in Ramsay scores between the two groups before analgesia, and 2 h and 3 h after analgesia ($p > 0.05$). In the research group, there were two parturients whose Ramsay score was 4 when the analgesia took effect, which showed that they were in sleep state, but were easy to wake up. There were no mothers with Ramsay score ≥ 4 in the control group. From Table 4, the VAS score of the research group was substantially higher than that of the control group at the onset of analgesia, and 1, 2, and 3 h after analgesia, and the differences were significant ($p < 0.05$). One hour after analgesia, the VAS score of the research group showed an upward trend, while the VAS score of the control group was relatively stable at each time point.

Comparison of vaginal delivery rate, labor process time, forceps delivery rate, cesarean section conversion rate, oxytocin use rate and adverse reactions between the research group and the control group

According to Table 5, there were no significant differences in vaginal delivery rate, total labor process, the first, the second and the third stage of labor, forceps delivery rate, conversion rate of cesarean section and oxytocin use rate between the research group and the control group ($p > 0.05$). There was no marked difference in the incidence of vomiting and pruritus between the two groups ($p > 0.05$). However, the incidence of dizziness in the research group (22.3%, 33/148) was substantially higher than that in the control group (2.7%, 4/259), and the difference was statistically significant ($\chi^2 = 39.537$, $p = 0.000$). The incidence of lower limb numbness in the research group (0.7%, 1/149) was markedly lower than that in the control group (5.8%, 15/259), and the difference was also statistically significant ($\chi^2 = 7.132$, $p = 0.007$).

Comparison of Apgar score and UA blood gas value between research group and control group

According to Table 6, the Apgar score and UA blood gas value of newborns in the research group and the control group were found to be within the normal range at 1 min

Table 5. Delivery process, forceps delivery, cesarean section rate and adverse reactions in the two groups [cases (%)]			
Characteristics	**Research group (n = 148)**	**Control group (n = 259)**	**p value**
Cases of vaginal delivery [%]	129 (87.2%)	221 (85.3%)*	< 0.01*
Total stage of labor [min]	527.6 ± 214.7	557.1 ± 208.7	0.24
First stage of labor [min]	478.6 ± 187.2	501.3 ± 211.3*	0.33
Second stage of labor [min]	42.7 ± 18.5	47.2 ± 21.1*	< 0.01*
Third stage of labor [min]	15.3 ± 5.3	14.7 ± 5.2	0.49
Cases of forceps delivery [%]	7 (4.7%)	12 (4.6%)*	< 0.01*
Cases of cesarean section [%]	15 (10.1%)	37 (14.3%)*	0.28
Cases of oxytocin [%]	64 (43.2%)	109 (42.1%)*	0.61
Adverse reactions			
Dizzy	33 (22.3%)	7 (2.7%)*	< 0.01*
Vomiting	8 (5.4%)	13 (5.0 %)*	< 0.01*
Itchy skin	3 (2.0%)	7 (2.7%)*	< 0.01*
Numbness of lower limbs	1 (0. 7%)	15 (5.8%)*	0.0

Values are expressed as mean (SD) or number (%); SD — standard deviation; *The difference was significant, if $p < 0.05$

Table 6. Comparison of neonatal condition between the research group and the control group			
Characteristics	**Research group (n = 148)**	**Control group (n = 259)**	**p value**
Apgar score			
Birth 1 min	9.6 ± 0.7	9.7 ± 0.5	1.00
Birth 5 min	9.8 ± 0.3	9.9 ± 0.4	1.00
Birth 1 min Apgar score ≤ 8 (cases [%])	10 (6.8)	13 (5.0)	0.51
UA blood gas analysis			
pH value	7.25 ± 0.63	7.29 ± 0.76	0.65
Residual alkali level	–5.21 ± 2.07	–5.43 ± 2.12	0.11

and 5 min after birth. There was no significant difference in Apgar score at 1 min and 5 min after birth, the percentage of Apgar score ≤ 8 at 1 min, the pH value and the residual alkali level between the two groups ($p > 0.05$).

Maternal satisfaction and the satisfaction of maternal family members with labor analgesia

According to Table 7, the maternal satisfaction rates and the satisfaction rates of maternal family members in the research group and the control group were all more than 90%. The maternal satisfaction rate in the research group and the control group was 93.9% (139/148) and 92.3% (240/259), respectively, with no significant difference between the two groups ($\chi^2 = 0.173$, $p = 0.712$). Also, the satisfaction rate of maternal family members in the research group and the control group was 93.2% (138/148) and 97.3% (252/259), respectively, with no significant difference between the two groups ($\chi^2 = 0.431$, $p = 0.517$).

DISCUSSION

There are some controversies about the safety of remifentanil in its use for patient-controlled intravenous labor analgesia for parturient and fetus. For example, previous studies have indicated that cesarean section under regional block and assisted analgesia with remifentanil 0.1 μg/kg could cause respiratory depression in parturient [5]. Also, according to Tveit et al. [6], remifentanil patient-controlled intravenous labor analgesia could cause maternal hypoxia saturation. Additionally, it has been reported that remifentanil background dose > 0.05 μg/(kg/min) increases the risk of maternal related complications [7]. However, Marr et al. [8] compared the efficacy of two regimens of intravenous PCA with remifentanil for labor analgesia and found that although the regimen used in Group A was associated with fewer side effects compared to the Group B dosing regimen, pain and satisfaction scores were similar in both groups, suggesting that remifentanil intravenous PCA is efficacious

Table 7. Maternal satisfaction and the satisfaction of maternal families in the research group and the control group about the labor analgesia (cases [%])

Characteristics	Research group (n = 148)	Control group (n = 259)	p value
Mothers			
Very satisfied	85 (57.4)	173 (66.8)*	< 0.01*
Satisfied	54 (36.5)	67 (25.9)	0.93
Generally satisfied	9 (6.1)	19 (7.3)*	< 0.01*
Maternal family members			
Very satisfied	91 (61.5)	189 (73.0)*	< 0.01*
Satisfied	47 (31.8)	63 (24.3)*	< 0.01*
Generally satisfied	10 (6.7)	7 (2.7)	0.71

Values are expressed as mean (SD) or number (%); 1. The satisfaction rate of the research group was (85 + 54) / 148 × 100% = 93.9%, and that of the control group was (173 + 67) / 259 × 100% = 92.3%. 2. The satisfaction rate of the family members in the research group was (91 + 47) / 148 × 100% = 93.2%, and that of the control group was (189 + 63) / 259 × 100% = 97.3%; SD — standard deviation; *The difference was significant, if $p < 0.05$

for labor analgesia as a bolus of 0.25 μg/kg^{-1}, with a lockout interval of two minutes and continuous infusion of 0.025–0.1 μg/kg^{-1}/min^{-1}. Bonner et al. pointed out that remifentanil PCA has been offered to women in labor since 2009 and they had not observed any critical incidents in over 130 patients using this mode of analgesia in their labor suite [9]. Thus, it appears that the adverse reactions reported in the literature were related to the unreasonable use of opioids and sedatives and the lack of close monitoring and had nothing to do with remifentanil.

In the present study, the background dose of remifentanil and PCA dose were 0.04 μg/(kg/min) and 0.4 μg/kg, respectively. Maternal ECG monitoring and fetal monitoring were implemented during the whole process of labor. Some pregnant women were given oxygen by conventional nasal catheter (3 L/min), and 24 h full-time anesthesiologists were present in the delivery room to accompany delivery one--on-one. There was no significant reduction in respiratory rate or desaturation in the research group and the control group. In the research group, SpO_2 decreased to 94% in only five cases, where the duration of this drop was short, and could be recovered after deep breathing. This observation was in line with the results of a recent meta-analysis that compared patient-controlled epidural analgesia and remifentanil intravenous labor analgesia [10, 11]. In the study of Stocki et al. [12], the primary study outcome was efficacy, which was assessed as hourly numerical rating scale (NRS) pain score (11-point NRS) and maternal satisfaction (11-point NRS). The secondary outcome was safety (*e.g.*, the lack of maternal apnea). In this study, supplementary oxygen was administered continuously during the respiratory monitoring period. During the first hour of analgesia, the heart rate, respiratory rate, SpO_2, and end-tidal CO_2, as an indication of apnea, were compared. Apnea lasting >40 seconds was managed by light stimulation by the attending anesthesiologist. The results obtained for the 40 women recruited (the remifentanil group [n = 19; 1 exclusion] and the epidural analgesia group [n = 20]) suggested that remifentanil was inferior to epidural analgesia for provision of labor analgesia. Nevertheless, we believe remifentanil does provide a satisfactory level of labor analgesia. Also, laboring women receiving remifentanil require suitable monitoring to detect and alert for apnea [12]. In the latter study, the fetuses of the two groups were monitored continuously, and there was no obvious pain-related abnormal fetal heart rate. Furthermore, according to some other studies, the incidence of abnormal fetal heart rate caused by remifentanil patient-controlled intravenous labor analgesia is very low, and there is no need for obstetric intervention [13, 14]. The Apgar score at 1 min and 5 min after birth in the research group of ref. was higher than or equal to 7. The Apgar score of 6.08% (9/148) newborns in the research group was less than or equal to 8 points at 1 min after birth. Compared with 5.02% (13/259) of the control group, the difference was not statistically significant ($p > 0.05$). Douma et al. [15] found that after one hour, visual analogue pain scores had decreased significantly in both groups (remifentanil: -3.8 ± 2.6, $p < 0.01$; epidural -6.7 ± 2.0, $p < 0.01$). The decrease in pain scores in the epidural group was significantly greater than the remifentanil group at all time intervals. The decrease in pain scores was sustained in the epidural group, whereas in the remifentanil group pain scores increased over time. Oxygen saturation was significantly lower in the remifentanil group after one hour of treatment compared to the epidural group ($95.2 \pm 2.4\%$ vs $99.0 \pm 1.1\%$, $p < 0.01$) [15]. Shen et al. [16] found that the mean (SD) remifentanil umbilical vein/maternal artery ratio in the PCA and infusion groups were 0.74 (0.45) vs 0.70 (0.52), respectively ($p = 0.776$) [16]. The mean (SD) umbilical artery/umbilical vein ratios were 0.31 (0.12) vs 0.26 (0.07), respectively ($p = 0.088$). Maternal and neonatal adverse reactions of remifentanil were similar between the two groups [16]. The results of the two above-mentioned

studies also suggested that the decrease of Apgar score at birth is not related to the mode of labor analgesia. The value of pH for UA blood in the research group and the control group was 7.25 ± 0.63 and 7.29 ± 0.76, respectively, and the residual alkali level was (–5.21 ± 2.07) mmol/L and (–5.43 ± ± 2.12) mmol/L, respectively. There was no significant difference in the pH value and the residual alkali level between the two groups ($p > 0.05$). Kan et al. [5] have proved that remifentanil is easy to pass through the placenta, but it can be quickly metabolized in the fetus without causing neonatal respiratory depression [17]. Nonetheless, the author still suggested that in the application of remifentanil patient-controlled intravenous labor analgesia one should provide perfect fetal monitoring measures and necessary neonatal rescue equipment in the delivery room, which can quickly respond to neonatal asphyxia and resuscitation.

In the preset study, the onset time of analgesia in the research group was (0.97 ± 0.08) min, which was significantly shorter than that in the control group (15.74 ± 1.91) min ($p < 0.05$). Thus, in situations of rapid progression of labor, especially when the diameter of uterine orifice is more than 8 cm, the use of remifentanil for patient-controlled labor analgesia could be prioritized by the anesthesiologist.

It is believed that remifentanil low background dose infusion has a relatively stable analgesic effect and can reduce the number of PCA [18, 19]. In the present study, the pain relief effect of the remifentanil group was lower than that of the control group ($p < 0.05$). In the research group, the VAS score of 6 parturients at 2 h after analgesia was ≥ 7. However, one hour after analgesia, the VAS score of the research group showed an upward trend; this is similar to what is found in related studies [20]. Nevertheless, the subjects of our research group generally believed that the pain during the whole labor process could be tolerated, which may be due to the sedation and euphoria effect caused by the opioids, which resulted in an improved maternal tolerance to pain [21]. According to Volmanen et al. [22], although the VAS score of the remifentanil group (7.2 points) was significantly higher ($p = 0.004$) than that of the patient-controlled epidural labor analgesia group (5.4 points), there was no significant difference in the scores of pain relief between the two groups (2.5 points and 2.8 points, respectively; $p = 0.11$).

In the present study, the maternal satisfaction rate and the satisfaction rate of maternal families in the research group were 93.9% and 93.2%, respectively, which were not significantly different ($p > 0.05$) from the values of 92.3% and 97.3% of the control group, respectively (Tab. 7). The fact that the satisfaction rate of the family members of the research group and the control group was slightly higher than the corresponding maternal satisfaction rates might indicate that once the pain of the parturient can be tolerated and properly sedated the anxiety of the family members could also be appropriately relieved, and they are willing to accompany the parturient to experience the whole childbirth process [23, 24]. However, Freeman et al. [25] found that the results of time weighted evaluation showed that the satisfaction rate of the patient-controlled intravenous analgesia (remifentanil) group was lower than that of the patient-controlled epidural analgesia group, and the difference was significant ($p < 0.05$) [25]. Thus, this issue requires further investigation.

In the present study, there were no significant differences in the time of labor, oxytocin use rate, forceps delivery rate and conversion rate between the research group and the control group ($p > 0.05$) (Tab. 5). The Ramsay scores at the onset of analgesia and 1 h after analgesia in the research group were higher than those in the control group ($t = = 9.997, 10.411$, $p = 0.000$). The incidence of dizziness in the research group (22.3%) was significantly higher than that in the control group (2.7%) ($p < 0.05$). Parturient felt dizzy and had drowsiness, but this kind of drowsiness makes the parturient feel comfortable. There was no significant difference in the incidence of vomiting and pruritus between the two groups ($p > 0.05$). At the first day of postpartum follow-up, it was found that 5.8% (15/259) of the control group had lower limb numbness, which was substantially higher than 0.7% (1/148) of the research group, and the difference was statistically significant ($p < 0.05$).

In conclusion, we should say that the method of labor analgesia with remifentanil background dose of 0.04 μg/ /(kg/min) and PCA dose of 0.4 μg/kg is safe for pregnant women and newborns. Although the analgesic effect is not as accurate and stable as that of patient-controlled epidural analgesia, it can still obtain higher satisfaction of mothers and their families. It can be used as an effective replacement for patient-controlled epidural analgesia in parturients with contraindications of spinal block, refusal of epidural puncture or unsatisfactory coordination of anesthesia position, especially for those with rapid progress of labor [26]. During the implementation of this method of labor analgesia, one gives maternal oxygen, provide perfect and continuous maternal and fetal monitoring measures [27], implement doula one-to-one delivery support [28], provide 24 h full-time anesthesiologists in the delivery room [29], and prepare for neonatal asphyxia resuscitation to the greatest extent to ensure the safety of the mothers and the newborn infants [30].

Article informations and declarations

Ethics approval and consent to participate

The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was

approved by the Human Ethics Committee of Shanghai First Maternity and Infant Hospital Ethics committee. Written informed consent was obtained from the individual or her guardian participants.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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Authors' contributions

HBL: Funding acquisition; Project administration; Writing--original draft. HL: Formal analysis; Investigation; Writing the review of literature and editing. YBY: Data curation; Formal analysis. YL: Validation; Writing the review of literature and editing.

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Conflict of interests

The authors declare that they have no competing interests.

REFERENCES

1. Althaus J, Wax J. Analgesia and anesthesia in labor. Obstet Gynecol Clin North Am. 2005; 32(2): 231–244, doi: 10.1016/j.ogc.2005.01.002, indexed in Pubmed: 15899357.
2. Logtenberg S, Oude Rengerink K, Verhoeven CJ, et al. Labour pain with remifentanil patient-controlled analgesia versus epidural analgesia: a randomised equivalence trial. BJOG. 2017; 124(4): 652–660, doi: 10.1111/1471-0528.14181, indexed in Pubmed: 27348853.
3. Schnabel A, Hahn N, Broscheit J, et al. Remifentanil for labour analgesia: a meta-analysis of randomised controlled trials. Eur J Anaesthesiol. 2012; 29(4): 177–185, doi: 10.1097/EJA.0b013e32834fc260, indexed in Pubmed: 22273829.
4. Melber AA. Remifentanil patient-controlled analgesia (PCA) in labour - in the eye of the storm. Anaesthesia. 2019; 74(3): 277–279, doi: 10.1111/anae.14536, indexed in Pubmed: 30549009.
5. Kan RE, Hughes SC, Rosen MA, et al. Intravenous remifentanil: placental transfer, maternal and neonatal effects. Anesthesiology. 1998; 88(6): 1467–1474, doi: 10.1097/00000542-199806000-00008, indexed in Pubmed: 9637638.
6. Tveit TO, Seiler S, Halvorsen A, et al. Labour analgesia: a randomised, controlled trial comparing intravenous remifentanil and epidural analgesia with ropivacaine and fentanyl. Eur J Anaesthesiol. 2012; 29(3): 129–136, doi: 10.1097/EJA.0b013e32834dfa98, indexed in Pubmed: 22249153.
7. Balki M, Kasodekar S, Dhumne S, et al. Remifentanil patient-controlled analgesia for labour: optimizing drug delivery regimens. Can J Anaesth. 2007; 54(8): 626–633, doi: 10.1007/BF03022956, indexed in Pubmed: 27771888.
8. Marr R, Hyams J, Bythell V. Cardiac arrest in an obstetric patient using remifentanil patient-controlled analgesia. Anaesthesia. 2013; 68(3): 283–287, doi: 10.1111/anae.12099, indexed in Pubmed: 23294158.
9. Bonner JC, McClymont W. Respiratory arrest in an obstetric patient using remifentanil patient-controlled analgesia. Anaesthesia. 2012; 67(5): 538–540, doi: 10.1111/j.1365-2044.2011.06997.x, indexed in Pubmed: 22268797.
10. Liu ZQ, Chen XB, Li HB, et al. A comparison of remifentanil parturient-controlled intravenous analgesia with epidural analgesia: a meta-analysis of randomized controlled trials. Anesth Analg. 2014; 118(3): 598–603, doi: 10.1213/ANE.0000000000000077, indexed in Pubmed: 24557106.
11. Lee M, Zhu F, Moodie J, et al. Remifentanil as an alternative to epidural analgesia for vaginal delivery: A meta-analysis of randomized trials. J Clin Anesth. 2017; 39: 57–63, doi: 10.1016/j.jclinane.2017.03.026, indexed in Pubmed: 28494909.
12. Stocki D, Matot I, Einav S, et al. A randomized controlled trial of the efficacy and respiratory effects of patient-controlled intravenous remifentanil analgesia and patient-controlled epidural analgesia in laboring women. Anesth Analg. 2014; 118(3): 589–597, doi: 10.1213/ANE.0b013e3182a7cd1b, indexed in Pubmed: 24149580.
13. Volikas I, Butwick A, Wilkinson C, et al. Maternal and neonatal side-effects of remifentanil patient-controlled analgesia in labour. Br J Anaesth. 2005; 95(4): 504–509, doi: 10.1093/bja/aei219, indexed in Pubmed: 16113038.
14. Tveit TO, Halvorsen A, Seiler S, et al. Efficacy and side effects of intravenous remifentanil patient-controlled analgesia used in a stepwise approach for labour: an observational study. Int J Obstet Anesth. 2013; 22(1): 19–25, doi: 10.1016/j.ijoa.2012.09.003, indexed in Pubmed: 23151415.
15. Douma MR, Middeldorp JM, Verwey RA, et al. A randomised comparison of intravenous remifentanil patient-controlled analgesia with epidural ropivacaine/sufentanil during labour. Int J Obstet Anesth. 2011; 20(2): 118–123, doi: 10.1016/j.ijoa.2010.11.009, indexed in Pubmed: 21376564.
16. Shen MK, Wu ZF, Zhu AB, et al. Remifentanil for labour analgesia: a double-blinded, randomised controlled trial of maternal and neonatal effects of patient-controlled analgesia versus continuous infusion. Anaesthesia. 2013; 68(3): 236–244, doi: 10.1111/anae.12098, indexed in Pubmed: 23294132.
17. Daly O, Kelly KP, McCormack JG, et al. Remifentanil PCA in labour. Anaesthesia. 2013; 68(7): 780–781, doi: 10.1111/anae.12339, indexed in Pubmed: 24044396.
18. D'Onofrio P, Novelli AM, Mecacci F, et al. The efficacy and safety of continuous intravenous administration of remifentanil for birth pain relief: an open study of 205 parturients. Anesth Analg. 2009; 109(6): 1922–1924, doi: 10.1213/ane.0b013e3181acc6fc, indexed in Pubmed: 19641051.
19. Marwah R, Hassan S, Carvalho JCA, et al. Remifentanil versus fentanyl for intravenous patient-controlled labour analgesia: an observational study. Can J Anaesth. 2012; 59(3): 246–254, doi: 10.1007/s12630-011-9625-0, indexed in Pubmed: 22057875.
20. Lu G, Yao W, Chen X, et al. Remifentanil patient-controlled versus epidural analgesia on intrapartum maternal fever: a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2020; 20(1): 151, doi: 10.1186/s12884-020-2800-y, indexed in Pubmed: 32164593.
21. Birnbach DJ, Ranasinghe JS. Is remifentanil a safe and effective alternative to neuraxial labor analgesia? It all depends. Anesth Analg. 2014; 118(3): 491–493, doi: 10.1213/ANE.0000000000000117, indexed in Pubmed: 24557091.
22. Volmanen P, Sarvela J, Akural EI, et al. Intravenous remifentanil vs. epidural levobupivacaine with fentanyl for pain relief in early labour: a randomised, controlled, double-blinded study. Acta Anaesthesiol Scand. 2008; 52(2): 249–255, doi: 10.1111/j.1399-6576.2007.01509.x, indexed in Pubmed: 18005381.
23. Stourac P, Kosinova M, Harazim H, et al. The analgesic efficacy of remifentanil for labour. Systematic review of the recent literature. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2016; 160(1): 30–38, doi: 10.5507/bp.2015.043, indexed in Pubmed: 26460593.
24. Frauenfelder S, van Rijn R, Radder CM, et al. Patient satisfaction between remifentanil patient-controlled analgesia and epidural analgesia for labor pain. Acta Obstet Gynecol Scand. 2015; 94(9): 1014–1021, doi: 10.1111/aogs.12694, indexed in Pubmed: 26073456.
25. Freeman LM, Bloemenkamp KW, Franssen MT, et al. Patient controlled analgesia with remifentanil versus epidural analgesia in labour: randomised multicentre equivalence trial. BMJ. 2015; 350: h846, doi: 10.1136/bmj.h846, indexed in Pubmed: 25713015.
26. Ohashi Y, Baghirzada L, Sumikura H, et al. Remifentanil for labor analgesia: a comprehensive review. J Anesth. 2016; 30(6): 1020–1030, doi: 10.1007/s00540-016-2233-y, indexed in Pubmed: 27619509.
27. Jelting Y, Weibel S, Afshari A, et al. Patient-controlled analgesia with remifentanil vs. alternative parenteral methods for pain management in labour: a Cochrane systematic review. Anaesthesia. 2017; 72(8): 1016–1028, doi: 10.1111/anae.13971, indexed in Pubmed: 28695584.
28. Logtenberg SLM, Vink ML, Godfried MB, et al. Serious adverse events attributed to remifentanil patient-controlled analgesia during labour in The Netherlands. Int J Obstet Anesth. 2019; 39: 22–28, doi: 10.1016/j.ijoa.2018.10.013, indexed in Pubmed: 30509681.
29. Van de Velde M. Patient-controlled intravenous analgesia remifentanil for labor analgesia: time to stop, think and reconsider. Curr Opin Anaesthesiol. 2015; 28(3): 237–239, doi: 10.1097/ACO.0000000000000191, indexed in Pubmed: 25827284.
30. Ortiz JU, Hammerl T, Wasmaier M, et al. Influence of Different Methods of Intrapartum Analgesia on the Progress of Labour and on Perinatal Outcome. Geburtshilfe Frauenheilkd. 2019; 79(4): 389–395, doi: 10.1055/a-0774-8617, indexed in Pubmed: 31000884.